AD_____

AWARD NUMBER: W81XWH-16-1-0015

TITLE: Patterns of Tinnitus and Hearing Loss Secondary to Blast Injury

PRINCIPAL INVESTIGATOR: Dewleen G. Baker, M.D.

RECIPIENT: Veterans Medical Research Foundation
San Diego, CA 92161

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PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Veterans Medical Research Foundation
3350 La Jolla Village Drive (151A)
San Diego, CA 92161

8. PERFORMING ORGANIZATION REPORT NUMBER

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

This three-year study proposes to recall Marine and Navy participants of the Marine Resiliency Studies, who were deployed and subject to blast-induced TBI for permission to access past and current audiograms given by the DoD and DVA, and to participate in phone interviews and complete on-line questionnaires, among consenting participants, 200 individuals divided among four groups will be invited for on-site evaluations. The study groups will be: **Group 1:** Blast-exposed during deployment with post concussive symptoms (PCS), new onset and persistent tinnitus; **Group 2:** Blast-exposed PCS, no tinnitus; **Group 3**: No blast-exposure during deployment, but new tinnitus; **Group 4:** No blast exposure, no tinnitus.

The onsite evaluations will consist of a magnetoencephalography (MEG) scan, hearing tests, standard MRS interviews, neurocognitive tests and questionnaires, and tinnitus questionnaires. By comparing subjects with tinnitus and those without, we hope better characterize the symptoms of blast-related tinnitus when compared to tinnitus from other causes such as falls or chronic noise exposure. We hope to develop better ways make an objective test, or diagnosis for tinnitus in blast versus non-blast exposed individuals with tinnitus onset. Thus our ultimate goal is to characterize the areas of the brain specifically associated with tinnitus.

15. SUBJECT TERMS

Tinnitus, Traumatic Brain Injury, Magnetoencephalography

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER	19a. NAME OF RESPONSIBLE PERSON
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Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

   This three-year study proposes to recall Marine and Navy participants of the Marine Resiliency Study (MRS and MRS-II) who were deployed and subject to blast-induced TBI, who had agreed to be re-contacted for future studies, for permission to access past and current audiograms given by the DoD and DVA, and to participate in phone interviews and complete on-line questionnaires. Among consenting participants, 200 individuals divided among four groups will be invited to San Diego for on-site evaluations. The study groups will be: Group 1: Blast-exposed during deployment with post concussive symptoms (PCS), new onset and persistent tinnitus; Group 2: Blast-exposed PCS, no tinnitus; Group 3: No blast-exposure during deployment, but new tinnitus; Group 4: No blast exposure, no tinnitus. The onsite evaluations will consist of a magnetoencephalography (MEG) scan and hearing tests, and well as standard MRS interviews, neurocognitive tests and questionnaires, including tinnitus questionnaires. The MEG is an imaging study of the brain, very much like an MRI, but has distinct advantages. First, it measures the nerve tracts of the brain, as well as their firing sequence in millisecond time, and it has the advantage of being quiet, so inside scanner tests can be done to assess aspects of the tinnitus while the brain is being imaged. By comparing Service Members with tinnitus and those without, we hope better characterize the symptoms of blast-related tinnitus when compared to tinnitus from other causes such as falls or chronic noise exposure, and to identify the centers of the brain that contribute to, or constitute the source of tinnitus. By better characterizing tinnitus, and better understanding how the brain contributes to it, we hope to develop better ways make an objective test, or diagnosis for tinnitus in blast versus non-blast exposed individuals with tinnitus onset. We are hopeful that this knowledge will allow for development of treatments, either medication or therapies based on modification or re-modeling of brain connections that are causing the tinnitus. Thus our ultimate goal is to characterize the areas of the brain specifically associated with tinnitus so as to formulate purposeful and effective treatment for this potentially devastating syndrome.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

   Tinnitus, Traumatic Brain Injury, Magnetoencephalography

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

   What were the major goals of the project?
   List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion

Specific Aim 1: We propose to analyze already available DVA and DoD medical data and audiology exams and to administer a brief interview and questionnaires (Primary Aims 1 and 2).	**Timeline**	**VASDHS**	**UCSD***	**Percent Completion by Year One**
Major Task 1: Obtain Local site IRB approval and Military IRB approval Coordinate Study Staff and Materials for Data Collection	Months			
Subtask 1: Refine eligibility criteria, exclusion criteria, screening protocol and finalize consent form & human subjects protocol	1-3 months	ASI	N/A	100%
Subtask 2: Prepare and submit Research Protocol and Regulatory Documents for local IRB Review	1-3 months	ASM	N/A	100%
Subtask 3: Prepare and submit Research Protocol and Regulatory Documents for HRPO IRB Review	1-3 months	ASM	N/A	100%
Subtask 4: Prepare and submit Research Protocol and Regulatory Documents for Military IRB Review	1-4 months	ASM	N/A	80%
Subtask 5: Submit amendments, adverse events and protocol deviations as needed	As Needed	ASM	N/A	N/A
Subtask 6: Submit annual IRB report for continuing review, milestone DOD reporting, and other agency reporting (VA, HRPO, CDMRP, etc)	Annually	ASM	N/A	N/A
Subtask 7: Hire staff and complete trainings and coordinate for space allocation for new staff	1-3 months	AP	N/A	95%
Subtask 8: Coordinate training of staff and technicians 100% concordance (inter-rater reliability)	1-6 months	AP/AD	N/A	100%
Subtask 9: Obtain all materials for data collection, create database, standard operating procedure and forms, and finalize all data collection preparation	1-6 months	ASM	N/A	100%
Milestone Achieved: Local IRB, HRPO IRB, and Military IRB approval at VASDHS	at 4 months	ASM	N/A	66%
Milestone Achieved: Research staff hired and trained and all materials ready for data collection	at 6 months	AP/AD	N/A	100%
Major Task 2: Data Collection and Data Entry				
Contact eligible participants and complete interview and questionnaires	6-24 months	ASP	N/A	0%
Subject data entry into study database	6-24 months	AD	N/A	0%
Audit and Clean Entered Subject Data, prepare for analysis	6-24 months	AD	N/A	0%
Milestone Achieved: All data is collected, entered, and prepared for analysis	at 24 months	ASP	N/A	0%
Major Task 3: Data Analysis and Dissemination of Study Findings				
Subtask 1: Finalizing data auditing and cleaning for statistical analysis	12-14 months	ASI	N/A	0%
Subtask 2: Perform all statistical analyses according to protocol, share output and finding with all investigators	12-36 months	ASI	N/A	0%
Subtask 3: Investigators and personnel to prepare for dissemination of findings (abstracts, presentation, publications, DOD)	12-36 months	ASI	N/A	0%
Milestone(s) Achieved: Data Analysis and Dissemination of Study Findings	at 36 months	ASI	N/A	0%
Specific Aim 2: We propose to invite four groups of participants to San Diego for more comprehensive assessment, audiogram, a tinnitus questionnaire, and MEG scan (200 subjects). (Aims 3)	**Timeline**	**VASDHS**	**UCSD***	**Percent Completion by Year One**
Major Task 1: Obtain Local site IRB approval and Military IRB approval Coordinate Study Staff and Materials for Data Collection	Months			
Subtask 1: Refine eligibility criteria, exclusion criteria, screening protocol and finalize consent form & human subjects protocol	1-3 months	ASI	N/A	100%
Subtask 2: Prepare and submit Research Protocol and Regulatory Documents for local IRB Review	1-3 months	ASM	N/A	100%
Subtask 3: Prepare and submit Research Protocol and Regulatory Documents for HRPO IRB Review	1-3 months	ASM	N/A	100%
Subtask 4: Prepare and submit Research Protocol and Regulatory Documents for Military IRB Review	1-4 months	ASM	N/A	80%

Subtask 5: Submit amendments, adverse events and protocol deviations as needed	As Needed	ASM	N/A	N/A
Subtask 6: Submit annual IRB report for continuing review, milestone DOD reporting, and other agency reporting (VA, HRPO, CDMRP, etc)	Annually	ASM	N/A	N/A
Subtask 7: Hire staff and complete trainings and coordinate for space allocation for new staff	1-3 months	AP	N/A	100%
Subtask 8: Coordinate training of staff and technicians 100% concordance (inter-rater reliability)	1-6 months	AP/AD	N/A	100%
Subtask 9: Obtain all materials for data collection, create database, standard operating procedure and forms, and finalize all data collection preparation	1-6 months	ASM	N/A	100%
Milestone Achieved: Local IRB, HRPO IRB, and Military IRB approval at VASDHS	at 4 months	ASM	N/A	66%
Milestone Achieved: Research staff hired and trained and all materials ready for data collection	at 6 months	AP/AD	N/A	100%
Major Task 2: Data Collection in San Diego and Data Entry				
Contact eligible participants, coordinate travel to San Diego for completion of assessment	6-30 months	ASP	ASP	0%
Subject data entry into study database	6-30 months	AD	N/A	0%
Audit and Clean Entered Subject Data, prepare for analysis	6-32 months	AD	N/A	0%
Milestone Achieved: All data is collected, entered, and prepared for analysis	at 12 months	ASP	N/A	0%
Major Task 3: Data Analysis, Dissemination of Study Findings, and Study Close Out and Final Reports				
Subtask 1: Finalizing data auditing and cleaning for statistical analysis	30-32 months	ASI	N/A	0%
Subtask 2: Perform all statistical analyses according to protocol, share output and finding with all investigators	30-36 months	ASI	N/A	0%
Subtask 3: Investigators and personnel to prepare for dissemination of findings (abstracts, presentation, publications, DOD)	30-36 months	ASI	N/A	0%
Subtask 4: Finalize and submit all study findings to appropriate scientific meetings, publications, etc	32-36 months	ASI	N/A	0%
Subtask 5: Investigators and personnel to prepare and submit final reports to corresponding agencies (DOD, VA, HRPO, etc)	32-36 months	ASI	N/A	0%
Milestone(s) Achieved: Data Analysis and Dissemination of Study Findings	at 36 months	ASI	N/A	0%
Milestone(s) Achieved: Final Reports Submitted to appropriate agencies	at 36 months	ASI	N/A	0%

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

1) Major activities: We have completed all sub-categories under Specific Aim 1, Major task 1, 1 except for annual renewal of the IRB, which is not yet necessary, and have begun and are accomplishing Aim, 1, Major task 2. Specifically, we have trained of staff and technicians listed in the third quarterly report, obtained IRB approvals to carry out the study, procured all materials for data collection for this fiscal year, and finalized our study entry database and standard

operating procedures. At our third quarter report, we noted that we replaced one of two staff members originally hired for the study; the new staff member is now fully trained, having completed all necessary study and VA trainings and certifications, and is currently in process of completing all cross trainings. In regard to Aim 1, Major task 2: We have begun contact, questionnaires, and interview of eligible participants for enrollment. To accomplish Major task 2, we upgraded our contact information, having found that the contact information that we had on file for the subjects from their previous participation in the Marine Resiliency Study was outdated. The majority of contact information that we had gathered for Marines during their previous participation was during their active duty status in the United States Marine Corps. Upon being presented with this problem, the study team made contact with various Veteran Affairs resources in order to obtain updated contact information for our potential, eligible subjects. Ultimately we were granted access to the Joint Legacy Viewer (JLV) system, which has updated contact information on MRS subjects. JLV is a web-based application co-developed by VA and the Department of Defense (DoD) for reviewing electronic health records from VA, DoD and Community Partners, and JLV provides an integrated, chronological view of health information from all sites where a patient has received care on a single screen, including DoD data. Moreover, JLV is in use at every VAMC and accessible from every VA site of care. Thus, we worked to obtain all VA IRB approvals to use this system, and completed required VA online trainings on its use so that MRS staffs have access to this system. As part of our IRB approval for use of the system, it was requested that we provide all potential subjects a study invitation letter introducing the tinnitus study, prior to making telephone contact. We have mailed out letters for a significant portion of our subject pool and are now in the process of consenting them for their participation to complete on line assessments (Study Aim 1). During this reporting period we have also completed all sub-categories under Aim 2, Major task 1 except for annual renewal of the IRB, which is not yet necessary. Specifically, we set up all protocols and equipment for audiology testing and imaging, as well as reviewed other data collection procedures and protocols required for on-site data collection. In particular, we have tested all audiology programs and MEG protocols with mock subjects and have made any necessary calibrations. The sound booth has been certified for quality control and all equipment has been permanently set up for data collection. We will continue to work closely with our scientific officer and the FITBIR team to ensure that all study milestones are met for the next reporting period. We do not anticipate that the minor setback of obtaining updated contact information will prevent us from completed our study goals nor will it impact our expenditures.

What opportunities for training and professional development has the project provided?

If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops,

conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.
Directly through training for the study we have provided the following training to our study Ph.D. psychologist who is completing interviews: 1) Training in delivery of the Clinician Administered PTSD Scale and 2) Training in giving neuropsychological testing

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We will continue recruitment and data collection in next reporting period.
There is nothing to report in terms of dissemination of information.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to Report

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

As noted above in section "3. Accomplishments" we found that the contact information that we had on file for the subjects from their previous participation in the Marine Resiliency Study while active duty was shown to be outdated. We have since obtained all VA IRB approvals to utilize the Joint Legacy Viewer database for the study and all staff has been granted individual access and has completed required VA online trainings on its use. Our

IRB required that we send all potential subjects an invitational letter introducing the study prior to making initial phone contact. Since accessing this database, we have been able to access up to date contact information for our subjects. We have contacted approximately 1/3 of our subject pool and are in the process of consenting them for their participation to complete study aim 1. We do not anticipate that the minor setback of obtaining updated contact information and an additional step of sending out an invitational letters prior to making phone contact prevent us from ultimately completing our study goals. The data collection for study aim 1 will slide so that it will overlap without study aim 2 so that we will be working on both concurrently as updated in the statement of work above.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals.

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted,*

awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).

Nothing to Report

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to Report

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to Report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**

  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

  - *data or databases;*
  - *biospecimen collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award).*

Name:	Dewleen Baker M.D.
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	0000-0002-1736-9838
Nearest person month worked:	3 CM
Contribution to Project:	Dr. Baker has overseen refinement of eligibility criteria, exclusion criteria, the screening protocol and finalization of the consent form & human subject's

protocol as well as ensured that the study hits all quarterly milestones during this reporting period.

Name: Caroline Nievergelt, Ph.D.
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0001-5766-8923
Nearest person month worked: 1.09 CM
Contribution to Project: Dr. Nievergelt has assisted in refinement of eligibility criteria, exclusion criteria, the screening protocol and finalization of the consent form & human subject's protocol, and the design of the overall study during this reporting period.

Name: Mingxiong Huang, Ph.D.
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 1.35 CM
Contribution to Project: Dr. Huang supervised MEG data acquisition equipment set up and programming, provided MEG trainings to all MEG operators, and served as the MEG lead this reporting period.

Name: Victoria Risbrough, Ph.D.
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 1.8 CM
Contribution to Project: Dr. Risbrough has assisted in refinement of eligibility criteria, exclusion criteria, the screening protocol and finalization of the consent form & human subject's protocol, and the design of the overall study during this reporting period.

Name: Royce Clifford, M.D
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0002-5515-4336
Nearest person month worked: 1.8 CM
Contribution to Project: Dr. Clifford has assisted in refinement of eligibility criteria, exclusion criteria, the screening protocol and finalization of the consent form & human subject's protocol, as well as set up all equipment related to audiology exam during this reporting period.

Name: Kate Yurgil, Ph.D.
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0003-0651-5219
Nearest person month worked: 1.8 CM
Contribution to Project: Dr. Yurgil has assisted in refinement of eligibility criteria, exclusion criteria, the screening protocol and finalization of the consent form & human subject's protocol, and the design of the overall study during this reporting period.

Name: Dean Acheson, Ph.D.
Project Role: Neurocognition Battery Expert

Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 1.5 CM
Contribution to Project: Mr. Acheson has performed work on the study database design, and the Neurocognition battery programming and its design this submission this reporting period.

Name: Andrew De La Rosa
Project Role: Data Manager
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 2.39 CM
Contribution to Project: Mr. Delarosa has performed work on the study recruitment materials, study databases, and local VA IRB and R&D submissions as well as the HRPO submission during this reporting period.

Name: Adam Maihofer
Project Role: Research Associate
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 2.46 CM
Contribution to Project: Mr. Maihofer has performed work on the study database design this submission this reporting period.

Name: Anjana Patel
Project Role: Project Manager
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 1.2 CM
Contribution to Project: Ms. Patel has performed work on the study recruitment materials, study databases, staff hiring, staff training, equipment procurement, overall staff supervision, subject assessment planning, and local VA IRB and R&D submissions as well as the HRPO submission during this reporting period.

Name: Shetal Patel
Project Role: Research Associate
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 4.34 CM
Contribution to Project: Dr. Patel has performed work on the study recruitment materials, study databases, staff training, and local VA IRB and R&D submissions as well as the HRPO submission during this reporting period.

Name: Kathryn Spaventa-Vancil
Project Role: Research Associate
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 4.8 CM
Contribution to Project: Dr. Spaventa-Vancil has performed work on the study recruitment materials, study databases, and assisted with local VA IRB and R&D submissions as well as the HRPO submission during this reporting period.

Name: Dhaval Patel
Project Role: Research Associate
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 1.8 CM
Contribution to Project: Mr. Patel has performed work on the study recruitment materials, study databases, and assisted with local VA IRB and R&D submissions as well as the HRPO submission during this reporting period

Name: Meegin Kincaid
Project Role: Research Associate
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 1.45 CM
Contribution to Project: Ms. Kincaid has performed work on the study recruitment materials, study databases, and assisted with local VA IRB and R&D submissions as well as the HRPO submission during this reporting period

Name: Bruna Cuccurazzu
Project Role: Research Assistant
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 2.27 CM
Contribution to Project: Mr. Cuccurazzu has performed work on the study recruitment materials, study databases, and assisted with all other preparation for data collection

Name: Charles Mayer
Project Role: Research Associate
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 4.04 CM
Contribution to Project: Mr. Mayer performed work on the study recruitment materials, study databases, and assisted with all other preparation for data collection.

Name: Michelene Wasil
Project Role: Research Associate
Researcher Identifier (e.g. ORCID ID): Not applicable
Nearest person month worked: 1.69 CM
Contribution to Project: Ms. Wasil performed work on the study recruitment materials, study databases, and assisted with local VA IRB and R&D submissions as well as the HRPO submission during this reporting period.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not

necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

N/A

Patterns of tinnitus and hearing loss secondary to blast injury

Log Number: MR141217

Funding Opportunity Number: W81XWH-14-CRMRP-NSRRA

PI: Dewleen G. Baker, M.D. **Org:** Veterans Medical Research Foundation **Award Amount:** $1,499,323

Study/Product Aim(s)

• To test the effects of blast-related TBI on hearing loss, we will obtain audiology data, current TBI status, and use annotated MRS data to determine the effect of TBI on hearing loss.

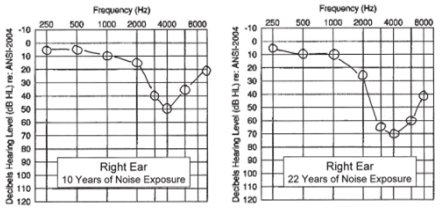
•To replicate and quantify further our previous work on PTSD, TBI, and tinnitus, we will use audiology data, current TBI status, tinnitus severity scores along with annotated MRS data to determine the effects of deployment-related TBI on tinnitus symptom severity as measured by the tinnitus functional index (TFI), controlling for relevant variables, i.e. prior noise exposure, prior hearing loss, and PTSD status.

• To compare 4 subgroups with blast exposure and ongoing TBI symptoms and without), post-concussive symptoms and tinnitus and without, we will examine MEG resting-state signals as well as MEG responses evoked by auditory stimuli in individuals to elucidate the neural mechanisms of tinnitus related to blast, and will relate MEG findings to TFI scores, audiograms, cognition and behavioral measures.

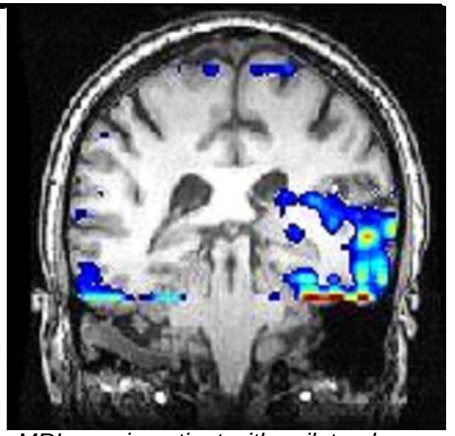
Approach

• To use extend MRS data collection to objectively measure tinnitus and hearing loss, we will contact MRS participants for consent to use audiogram data, administer an interview (TBI and PTSD status) and questionnaires (TFI), and recruit a subsample of 200 Marines (blast plus ongoing TBI symptoms versus no-blast) and (tinnitus versus tinnitus) for on-site collection of MEG scans and quantitative audiogram data.

• Primary outcome measures: Audiograms data, TFI score, MEG data.



Classic “notch” at 4000Hz from noise, which increases with exposure to noise. We hypothesize a “notch” at 6000Hz in blast-related TBI



MEG coherence mapping image overlaid on MRI scan in patient with unilateral tinnitus shows left auditory cortex is significantly more active. (Courtesy of Henry Ford Hospital).

Accomplishment: To define a pattern of blast-related hearing loss and tinnitus, distinct from non-blast, which could serve as a biomarker of diagnosis and basis for treatment

Timeline and Cost

Activities CY	1	2	3
Hire staff, prepare for data collection, obtain all regulatory approvals			
DOEHRS and audiogram data, analyze for pattern of hearing loss			
Perform MEG for tinnitus and blast patterns in 50 per group			
Analyze Tinnitus Data, Dissemination of Study Findings, and Final Reports			
Estimated Budget ($1.5MM)	**$465K**	**$550K**	**$484K**

Updated: January 24, 2017

Goals/Milestones

CY1 Goals– Initiate Study and Data Aggregation

- ❑Hire, train staff, buy equipment, finalize and submit regulatory and human subjects protocols to corresponding IRBs
- ❑Obtain local and Military IRB approvals
- ❑Acquire DOEHRS and audiogram data, analyze for pattern of hearing loss

CY2 Goals – Data Collection and Analyze Data for Aims 1 and 2

- ❑MEG studies on MRS participants
- ❑Audiograms, TBI and PTSD questionnaires

CY3 Goals – Data Collection, Score and Analyze Data, and Final Report

- ❑Analysis of data and published reporting of results

Comments/Challenges/Issues/Concerns

- None applicable with LOI application

Budget Expenditure to Date

Projected Expenditure: $464,899

Actual Expenditure: $451,364